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EXAMINER	
GOLDBERG, JEANINE ANNE	
ART UNIT	**PAPER NUMBER**
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/702,134	BOUKHAROV ET AL.	
	Examiner	Art Unit	
	Jeanine A. Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 8-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 8-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed December 7, 2006. Currently, claims 1, 8-12 are pending.

2. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. Any objections and rejections not reiterated below are hereby withdrawn.

   a. The 102 rejection previously of record has been withdrawn in view of the amendments to the claims.

3. This action is FINAL.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 1 and 8-12 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

The claimed subject matter is not supported by a specific, substantial, and credible asserted utility because the disclosed uses are generally applicable to broad classes of this subject matter. Further characterization of the claimed subject matter would be required to identify or reasonably confirm a real world use. The examiner does not find an adequate nexus between the evidence of record and the asserted properties of the claimed subject matter.

The specification teaches that SEQ ID NO 7212 is one of a group of over 50,000 large genomic fragments obtained from rice (see entire specification). The specification asserts that a variety of uses are applicable to all of the disclosed sequences, including use of the various sequences in genomic mapping, gene identification and analysis, plant breeding, preparation of expression constructs, preparation of transgenic plants, screening for traits, and determination of polymorphisms and of associations between polymorphisms and traits (see entire specification, particularly, e.g., pages 1, 12, and 18). However, the uses asserted in the specification are general utilities and methods of further research that are applicable to virtually any genomic nucleic acid from any plant. For example, any plant nucleic acid could be employed in genomic mapping, and any plant nucleic acid could be analyzed from the presence of genes (which genes could further be subjected to analysis); such general methods do not constitute substantial uses that are specific to one or more of the molecules disclosed by applicant.

Further, while such mapping and nucleic acid analysis might eventually result in the identification of, e.g., particular regulatory elements useful in recombinant expression methods or in preparation of transgenic plants, specific polymorphisms associated with specific traits, particular open reading frames encoding useful proteins, etc., such further research and experimentation on nucleic acids also constitutes a general utility, rather than a specific and substantial "real world" use. See *Brenner v. Manson*, 383 U.S. 519, 535-536, 148 USPQ 689, 696 (1966), noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful

conclusion". A patent is therefore not a license to experiment with the objective of eventually identifying a specific and substantial use for a product or method. With regard to SEQ ID NO: 7212 in particular, while the specification discloses that the sequence has been examined for homologies with known genes (see, e.g., Table 1), the specification does not provide any evidence that applicants have, e.g., identified within SEQ ID NO: 7212 any particular polymorphisms associated with a trait or traits, identified any particular promoters or regulatory elements useful in methods of recombinant gene expression, determined that any of the putative open reading frames in the sequence actually encodes a protein having a specific use, etc. Accordingly, the claimed invention is not supported by a specific, substantial and credible asserted utility.

With regard to the possibility that there may exist a well-established utility for the claimed invention, it is noted that SEQ ID NO: 7212 is free of the prior art. A search of the prior art indicates that SEQ ID NO: 7212 does contain a region of significant homology with a known molecule, specifically, with a rice cDNA encoding **gibberellin 20-oxidase** (GENBANK Accession No. U50333, February 1997). The table indicates that position 28572-30174 is probable gibberellin C-20 oxidase. However, an alignment of this cDNA with SEQ ID NO: 7212 reveals (in addition to multiple mismatches) multiple frameshifts within the coding sequence of the cDNA; accordingly, the prior art indicates that SEQ ID NO: 7212 and the prior art cDNA **do not** in fact **encode** the same protein. Thus, the prior art does not provide any evidence of a well-established utility for SEQ ID NO: 7212. The other proteins proposed to be encoded by 7212 similarly are not sufficient to provide utility. For example the Genbank X59270 is a spinach

chloroplast rps22 sequence which when Blasted does not have any significant similarity found. Moreover, the 279640 accession number is a protein sequence. The instant claims are drawn to nucleic acid sequences.

With regard to the rejection of claims 1 for lack of utility in the Office action of August 12, 2003, the response traversed the rejection on the following grounds. Applicant argues that the claimed invention possess numerous utilities, including those cited by the examiner in the Office action of August 12, 2003 (which utilities were identified by the examiner as being general utilities and methods of further research), as well as "obtaining protein molecules, determining the presence and/or identity of polymorphisms, measuring the levels of an mRNA in a sample, determining the location of a corresponding DNA sequence on a physical or genetic map, probing for other molecules, obtaining other nucleic acid molecules from the same species, obtaining related protein coding sequences, obtaining promoters and other flanking genetic elements, screening cDNA genomic libraries, obtaining nucleic acid homologs, detecting and characterizing gene expression, etc." The response further argues that the uses disclosed in the specification "are directly analogous to a microscope" which is useful "to identify and characterize the structure of biological tissues in a sample, cell, or organism," and urges therefore that "the presently disclosed sequences possess the requisite utility" under 35 U.S.C. 101. Applicant states that the examiner "suggests that the asserted utilities are legally insufficient simply because other molecules can be used for the same purpose" as the claimed molecules. Applicant urges that "there is no requirement of exclusive utility in the patent law," and states that "such an argument

implies that a new golf club has no legal utility because other golf clubs can be used for the same purpose." The response argues that the claimed molecules meet the utility requirement because they "will identify a unique subset of related sequences" which is "specific to the claimed sequences and cannot be identified by any generic nucleic acid molecule."

Applicant's arguments have been thoroughly considered but are not persuasive. First, with regard to the list of utilities recited by Applicant at pages 19-20 of the Response, it is noted that these utilities, like the other asserted utilities noted by the examiner in the Office action of August 12, 2003, constitute general utilities and methods of further research that are applicable to virtually any genomic nucleic acid from any plant. With regard to Applicant's argument that the claimed nucleic acids may be used "to identify and characterize other nucleic acid molecules within a sample, cell or organism" in a manner analogous to a microscope, this argument is not persuasive. Like the other general utilities discussed above, such a general use (in "identifying and characterizing" other nucleic acids) is applicable to virtually any genomic nucleic acid. While it is true that a microscope may be employed in identifying and characterizing tissues, this is also true of numerous types of equipment found routinely in laboratories, including gel electrophoresis apparatus, thermocyclers, vacuum blotters, etc.; all of these items may be used in various ways to achieve the general objective of "identifying and characterizing" biological tissues. However, a microscope is known to function in a particular way that differentiates it from these other types of equipment, and has a use in specific aspects of identification and characterization of tissues (e.g., visualization of

structures) that differs from the specific uses of other types of equipment that are also useful in "identifying and characterizing" tissues. Accordingly, in contrast to the molecules of the claims, a microscope is not merely a member of a large genus of items for which specific functions have yet to be identified, but rather a well characterized piece of laboratory equipment with a specific and substantial use. Applicant has yet to identify such a specific and substantial use for SEQ ID NO: 7212. Regarding Applicant's statement that the examiner "suggests that the asserted utilities are legally insufficient simply because other molecules can be used for the same purpose," it is noted that the examiner did not make such a statement, but rather suggested that uses that are generally applicable to any nucleic acid cannot be considered a specific and substantial use for a particular nucleic acid molecule. It is acknowledged that a variety of different types of golf clubs may be used to hit a golf ball. However, this use in performing a specific task (i.e., hitting a golf ball) differentiates golf clubs from other types of athletic equipment (for example, tennis racquets).

However, the instant specification does not disclose a substantial use that is specific either to SEQ ID NO: 7212 or, e.g., a group of molecules including SEQ ID NO: 7212 that would differentiate it from, for example, SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, etc. Further, while it is acknowledged that SEQ ID NO: 7212 could be used to differentiate, e.g., complements of SEQ ID NO: 7212 from complements of SEQ ID NO: 1, complements of SEQ ID NO: 2, etc., such a use is not specific and substantial unless a specific and substantial use for the molecule being detected has been identified. It is again noted that research and experimentation on nucleic acids constitutes a general

utility, rather than a specific and substantial "real world" use. See *Brenner v. Manson*, 383 U.S. 519, 535-536, 148 USPQ 689, 696 (1966), noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion". A patent is therefore not a license to experiment with the objective of eventually identifying a specific and substantial use for a product or method. Accordingly, Applicant's arguments are not persuasive.

Response to Arguments

The response filed December 7, 2006, June 12, 2006 and the appeal brief filed February 22, 2005 traverses this rejection. Appellant's arguments have been fully considered but are not persuasive for the reasons that follow.

The response filed December 7, 20006 and June 12, 2006 asserts that the specification clearly discloses that SEQ ID NO: 7212 contains sequences that encode numerous proteins. The copy of the Table kindly faxed to the Examiner illustrates many hypothetical and probable proteins within SEQ ID NO: 7212. As noted in the rejection, with regard to the possibility that there may exist a well-established utility for the claimed invention, it is noted that SEQ ID NO: 7212 is free of the prior art. A search of the prior art indicates that SEQ ID NO: 7212 does contain a region of significant homology with a known molecule, specifically, with a rice cDNA encoding **gibberellin 20-oxidase** (GENBANK Accession No. U50333, February 1997). The table indicates that position 28572-30174 is probable gibberellin C-20 oxidase. However, an alignment of this cDNA with SEQ ID NO: 7212 reveals (in addition to multiple mismatches) multiple frameshifts within the coding sequence of the cDNA; accordingly, the prior art indicates that SEQ ID

NO: 7212 and the prior art cDNA **do not** in fact **encode** the same protein. Thus, the prior art does not provide any evidence of a well-established utility for SEQ ID NO: 7212. The other proteins proposed to be encoded by 7212 similarly are not sufficient to provide utility. For example the Genbank X59270 is a spinach chloroplast rps22 sequence which when Blasted does not have any significant similarity found. Moreover, the 279640 accession number is a protein sequence. The instant claims are drawn to nucleic acid sequences. Thus, the skilled artisan would not be able use SEQ ID NO: 7212 without further experimentation to determine a real-world use. Each of the nucleic acids within 7212 does not provide a specific or substantial utility that could be used as discussed by the response.

The response of December 7, 2006 asserts that Applicant can establish utility by a reasonable correlation by relying on statistically relevant data documenting the activity of the compound or the composition, argument or by reasoning. Here, the applicants merely point to the examiners admission that there is significant homology with gibberellin 20-oxidase to support the correlation to gibberellin 20-oxidase. However, as pointed out by the alignment there a several single nucleotide differences and gaps which cause frameshifts in the nucleic acid. The instant specification fails to provide any analysis that the claimed nucleic acid encodes a gibberellin nucleic acid that functions as the well known gibberellin 20-oxidase. Furthermore, the claims encompass 90% identity such that mutants of the nucleic acid are encompassed. The examiner does not dispute that gibberellin 20-oxidase has utility, however the instant claimed nucleic acids have not been shown to have this same activity.

It is well known in the art that single nucleotide changes may alter the function, and/or truncate the protein. For example, Sickle-cell disease in humans is caused by a single nucleotide polymorphism (SNP). This SNP is responsible for sickle cell anemia. The beta-globin gene does not cause any apparent effects on the secondary, tertiary or quaternary structure of hemoglobin. However, it causes a severe condition which shortens the life span of people affected. Thus a single little change in a gene with significant homology does not have the same function and there is no reasonable correlation. http://en.wikipedia.org/wiki/Sickle-cell_disease

The response asserts that "applicants have met this part of the bargain- the present specification discloses nucleic acid molecule which, in their current form, provide at least one specific benefit to the public, for example, their use to encode a 30S Ribosomal protein S30, gibberellin C-20 oxidase and several receptor kinase-like proteins. This argument has been reviewed, but is not persuasive. What the instant application appears to have done was sequenced a very large segment of DNA from rice and provided the sequence. The sequence appears to contain portions which show some homology to know sequences, but the sequence does not contain these sequences, as noted above by the BLAST comparison. Therefore, the skilled artisan would be required to perform additional experimentation to carry out a real-world context of use. Therefore, transforming plants with these sequences or monitoring the expression of such proteins or mRNA associated with those proteins would not be specific or substantial.

With respect to Applicants arguments directed to Table 1 (page 4 of response filed December 7, 2006), asserting homology to SEQ ID NO: 7212 and other proteins, the search in the nucleic acid databases did not yield any similarity to these proteins. There is no evidence on the record direct to the homology or alignments of these known proteins with the claimed sequences.

At pages 4-5 the brief traverses that the lack of utility analysis misstates the asserted uses, ignores disclosed utilities, and misapplies the doctrine of "practical utility" and applies case law in support for the doctrine of "practical utility" and the requirement for "identifiable benefit". These arguments are not specifically drawn to the rejection set forth previously or above, and are an allegation. They are found non-persuasive and are reasonably an introductory summary set forth by the brief. As a preliminary matter, the rejections in this application are made in order to comply with office policy regarding the utility guidelines (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for Utility.). So to the extent that any argument conflicts with the guidelines, it will necessarily be non-persuasive.

Appellants assert at page 3 and pages 5-6, that they have met the conditions of providing the public with an invention having substantial utility wherein specific benefit exists in currently available form. Appellants state that, in particular, the claimed nucleic acids can be used to identify a polymorphism in a population of plants. However, this is not considered to be a specific and substantial utility. The utility is not specific because it is a property of all plant nucleic acids that they could be used to search for and try to identify a polymorphism. Further, the asserted utility is not substantial because it is a

utility that is performed only to accomplish additional research. All discussions regarding polymorphisms in the specification are generic in nature. The specification does not teach any particular polymorphisms in SEQ ID NO: 7212. The specification does not disclose an association between any particular polymorphisms and any phenotypic trait. Polymorphisms are naturally occurring variations within sequences, which themselves may not have any meaningful use. To determine whether a nucleic acid contains a polymorphism would first require comparing the sequence of SEQ ID NO: 7212 to other newly isolated nucleic acids. Then, upon identifying a nucleic acid variation, one would need to determine whether such a variation had any meaningful use – e.g., whether the variation was associated with a particular trait or characteristic of a particular strain of plant. Therefore, the nucleic acids of SEQ ID NO: 7212 may only be used to search for polymorphisms and if such polymorphisms are identified then the functional/biological activities of the polymorphisms could potentially be elucidated. Such research projects do not constitute a "real-world" use in currently available form.

As set forth in the MPEP (2107):

> On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":
>
> (A) Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved;
>
> (B) A method of treating an unspecified disease or condition;
>
> (C) A method of assaying for or identifying a material that itself has no specific and/or substantial utility;
>
> (D) A method of making a material that itself has no specific, substantial, and credible utility; and
>
> (E) A claim to an intermediate product for use in making a final product that has no specific, substantial and credible utility.

Each of these situations closely matches Appellant's disclosed uses. These uses do not define substantial utilities.

Further, MPEP 2107 states that:

> An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring.

However, in the present situation, the specification does not disclose a correlation between such polymorphisms and any conditions or traits.

Appellants assert that the use of the claimed nucleic acids to detect a polymorphism is analogous to the utilities associated with a microscope, i.e., the claimed nucleic acids may be used to locate and measure nucleic acid molecules in a sample, cell or organism. However, the use of a nucleic acid to detect a polymorphism is not considered to be analogous to the use of a microscope. The microscope can be used to immediately provide information. For instance, the microscope can be used to identify or distinguish between gram-positive and gram-negative bacteria. This use is well known and its benefits are immediately recognizable. The use of a nucleic acid to detect a polymorphism does not provide information of immediate benefit. If a researcher determines that a polymorphism is present, the researcher would not know what to do with this information since the specification has not disclosed a specific association between any particular polymorphisms and any particular traits. This situation is significantly distinct from a situation in which a nucleic acid is to be used to detect a previously disclosed polymorphism known to be associated with a specific trait.

In such a situation, the nucleic acid would have a specific and substantial utility because the information obtained by detecting the polymorphism is specific and of immediate benefit. In contrast, the present invention requires the researcher to first identify a new polymorphism and then determine whether this polymorphism is associated with any particular trait or condition. The information gained by detecting an unknown and uncharacterized polymorphism is not specific and not of immediate benefit.

As set forth above, the rejection is based on the finding that Appellants have not disclosed a substantial and specific or well-established utility for the claimed invention. The facts supporting this conclusion are clearly set forth throughout the rejection. The instant situation is analogous to that which was addressed in *Brenner v. Manson*, 148 USPQ 689 (1966) wherein the court held that 35 U.S.C. 101 requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that :

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility...[u]nless and until a process is refined and developed to this point where specific benefit exists in currently available form there is insufficient justification for permitting an appellant to engross what may prove to be a broad field...a patent is not a hunting license...[I]t is not a reward for the search, but compensation for its successful conclusion."

In the present situation, Appellants have not arrived at a "successful conclusion" as to the actual functional role or significance of the claimed nucleic acids. Without such information, the claimed nucleic acids can only be used as a starting point for conducting further experiments to arrive at a "successful conclusion."

Claim Rejections - 35 USC § 112- Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Additionally, claims 1 and 8-12 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The teachings of the specification and of the prior art do not enable one skilled in the art to use molecules having any "nucleic acid sequence of SEQ ID NO: 7212 or its complement" or molecules "capable of specifically hybridizing" to such molecules, or molecules that have between 90%-100% identity with SEQ ID NO: 7212.

Claim 1 as written is sufficiently broad so as to encompass any molecule "having a nucleic acid sequence of SEQ ID NO: 7212 or its complement" (i.e., any subsequence of the recited sequences, rather than the full length molecules). Accordingly, the claims are not limited to, e.g., nucleic acids encoding a protein with a particular biological activity, but rather embrace numerous other molecules. Further, the claims as written encompass subsequences of any length of SEQ ID NO: 7212 or its complement, and further embrace flanking sequences of unspecified length and identity.

Claims 8-12 encompass molecules that are 90%-100% identical to SEQ ID NO: 7212, and which also may be flanked by sequences of any length and identity. Thus, the claims as written encompass allelic and splice variants SEQ ID NO: 7212 and

fragments thereof, naturally and non-naturally occurring mutants of these sequence, variants isolated from other organisms, etc. In the approximately 69,000 bases of 7212, a sequence which is 90% identical would encompass a sequence with 6,900 differences. The specification has not disclosed a specific and substantial utility even for, e.g., a particular nucleic acid consisting of SEQ ID NO: 7212, and further does not teach a biological function for the large genus of molecules encompassed by the claims, or otherwise provided guidance with respect to how such molecules may be used in a utility meeting the requirements of 35 USC 101. Additionally, it is again noted that the prior art is silent with respect to SEQ ID NO: 7212.

With respect to the claims requiring percentage identity, it would be unpredictable for the skilled artisan to determine how to use the nucleic acid sequence which shares homology with the claimed sequence. The response asserts that SEQ ID NO: 7212 comprises known nucleic acids which encode proteins, however, in the event that the variation exists in these regions, the nucleic acid would not share structure with the asserted use. The skilled artisan would be required to perform unpredictable and undue experimentation to determine how to use nucleic acids which share only a percent identity with the claimed nucleic acid. Since the claimed nucleic acid itself does not have any use, it is further experimentation and trial and error research to determine how to use the sequences which are similar to those provided by SEQ ID NO:.

Accordingly, while one of skill in the art could conduct further experimentation aimed at, e.g., identifying a particular function for the molecules of the claims, such a

function is not presently known, and the outcome of such experimentation cannot be predicted. Thus, it would require undue experimentation to use the claimed invention.

Response to Arguments

The brief at page 13 states that this rejection is erroneous and has been overcome by the arguments stated above regarding utility. However, for the reasons set forth above, it is maintained that the uses asserted for the claimed invention are an object of study and are not specific, nor substantial. The specification cannot enable or teach one how to use the invention within 35 U.S.C. 112, first paragraph, if there is no patentable utility within 35 U.S.C. 101. Because there is no utility for the claimed invention for the reasons set forth above, it is maintained that the specification has not enabled the claimed invention.

Claim Rejections - 35 USC § 112-Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1 and 8-12 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The analysis used in this Written Description rejection follows the guidelines provided in the Federal Register, Vol. 66, No. 4, January 1, 2001, beginning at page 1099 (referred to in the rejection as "the guidelines.").

The guidelines direct one, for each claim, to determine **what the claim as a whole covers** (p. 1105, 2nd column).

Vas-Cath Inc. V. Mahurkar, 19 USPQ2b 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2b 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...' required a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

It is first noted that nucleic acids consisting of SEQ ID NO: 7212 meet the written description requirements. However, none of the instant claims are limited to such a

molecule. It is again noted that claim 1 as written encompasses any molecule "having a nucleic acid sequence of SEQ ID NO: 7212 or its complement" (i.e., any subsequence of the recited sequences, rather than the full length molecules). The claims are not limited to, e.g., nucleic acids sharing the same function as SEQ ID NO: 7212 or encoding a protein with a particular biological activity, but rather embrace numerous other molecules. Further, the claims as written encompass subsequences of any length of SEQ ID NO: 7212 or its complement, and further embrace flanking sequences of unspecified length and identity.

Claims 8-12 encompass molecules that are 90%-100% identical to SEQ ID NO: 7212, and which also may be flanked by sequences of any length and identity. Thus, the claims as written encompass allelic and splice variants SEQ ID NO: 7212 and fragments thereof, naturally and non-naturally occurring mutants of these sequence, variants isolated from other organisms, etc. However, the specification does not exemplify nucleic acids that have 90-99% identity with SEQ ID NO: 7212. Further, the claims recite open transitional language ("having"; "comprising"), and therefore include, e.g., molecules that are 90-100% identical with SEQ ID NO: 7212 and which further include undefined flanking sequences. As a result, the claims read on additional variants, mutants, homologues, etc., that differ completely from SEQ ID NO: 7212 with respect to both structure and function.

Next, the guidelines direct a review of the application to understand **how the application provides support for the claimed invention**.

The specification teaches a single molecule within the scope of the claimed invention, that is SEQ ID NO: 7212. The specification does not teach any variants of SEQ ID NO: 7212, nor does the specification teach any single nucleotide polymorphism within SEQ ID NO: 7212. Thus, the single molecule provided in the specification represents only one species within the vast genus claimed.

Considering then, the scope of the claims and the teachings of the specification, the guidelines direct one to **determine whether there is sufficient written description to inform a skilled artisan that applicant was in possession of the claimed invention as a whole** at the time the application was filed. The guidelines direct that such possession may be shown in many ways, including an actual reduction to practice, detailed drawings or in chemical formulas, and description of sufficient, relevant, identifying characteristics. In addition, for a claim drawn to a genus the requirement may be satisfied by description of a representative number of species, reduction to drawings, or by disclosure of other sufficient, relevant, identifying characteristics.

The instant specification does not provide sufficient written description to inform one of possession of the invention as a whole. There is actual reduction to practice of only a single embodiment within claims 1, 8-12. Reduction to practice of only a single embodiment is not reduction to practice of the entire scope of the claim, and thus, applicant has not met the written description requirement by reduction to practice.

The only structural chemical formula given in the specification is SEQ ID NO: 7212. For all of the rejected claims, only a partial structure representing the entire genus is given, that is SEQ ID NO: 7212. The teachings of the specification do not

couple this structure with any additional physical or chemical characteristics or functional characteristics. This structural formula represents only a single species of the claimed invention for claims 1, 8-12. As noted in this rejection, however, the claimed invention is quite broad in nature, and this single example is not a "representative number of species" since the entire genus of molecules encompassed within this genus is so broad and includes molecules of any possible function.

The level of skill in the art is quite high, but the unpredictability regarding the functioning of nucleic acid sequences upon modification is even higher. The function of a nucleic acid, with regard to a coding or non-coding function is highly sequence dependent. For example, the art teaches repeatedly that mutations in a critical region of a promoter element can destroy the ability of a construct to function in promotion. For example, Pietrzkowski *et al.* (Experimental Cell Research, 193, 283-290 (1991)) teaches that when synthetic promoters were produced wherein the sequence of an enhancer element was mutated, little to no promotion was observed from the constructs where the promoter was mutated (see for example Figure 6). Chan *et al.* (Plant Molecular Biology 46 :131-141, (2001)) teach that mutation in a critical XXIII element of the GAPB promoter abolished transcription completely (Figure 6), while mutations in other elements did not abolish activity (Figure 6). Thus, it is evident that it is highly unpredictable how promoter elements will respond to even very minor sequences changes. In addition, the order that promoter elements occur in a construct has an effect on the functionality of the promoter. Omilli *et al.* (Molecular and Cellular Biology, June 1986, p. 1875-1885) teach that the relative arrangement of promoter elements is a

critical factor contributing to the activity of the promoter (ABSTRACT, for example). In this case, there is no functional requirement given regarding the claimed nucleic acids, and thus the claimed nucleic acids encompass a wide variety of structurally distinct molecules whose function may or may not be associated with SEQ ID NO: 1 in the same manner.

Thus, having carefully considered all of these factors, it is concluded that the specification does not provide adequate written description for the claimed invention.

Response to Arguments

The response filed December 7, 2006 and the brief filed February 22, 2005 traverses the written description rejection. It is argued that the specification demonstrates that Appellant was in possession of the claimed genus of nucleic acid molecules. It is further asserted that the fact that the claims are joined with additional sequences, or complements of the recited sequence or nucleic aid molecules that share a claimed identity with the recited sequence does not mean that Appellant was any less in possession of the claimed nucleic acid molecules. This argument was thoroughly reviewed but was not found persuasive. The rejection is based on the fact that the claims include full length genomic sequences comprising the recited SEQ ID NO: 7212. With regard to claims 8-12, the claims further encompass sequences having 90% to less than 100% identity with SEQ ID NO: 7212 and sequences comprising these variant sequences. Thereby, the claims encompass mutants, allelic variants, splice variants and homologues of SEQ ID NO: 7212 which are not adequately described in the present specification.

Appellants state that the application describes more than just the nucleotide sequence of SEQ ID NO: 7212. It is asserted that the specification describes vectors comprising the claimed nucleic acid molecules, the addition of other nucleotides or detectable labels, fusion peptides, as well as sequences having particular sequence identity to claimed nucleic acid molecules. Appellants cite Enzo Biochem (Fed. Cir. 2002) as stating that the written inquiry is a factual one determined on a case-by-case basis and that, in a given disclosure, "it may well be that various subsequences, mutations, mixtures of those sequences are also described to one of skill in the art."

These arguments have been fully considered but are not persuasive. The genus of nucleic acids encompassed by the claims is extremely broad and is not limited to vectors comprising the nucleic acids or to nucleic acids comprising a label. The claims further encompass mutants, allelic variants, splice variants and homologues of SEQ ID NO: 7212. A general statement in the specification of a desire to obtain gene sequences, homologues from other species, mutated species, SNPs, polymorphic sequences, promoter sequences and exogenous sequences is not equivalent to providing a clear and complete description of specific sequences which fall within the claimed genus of nucleic acids. As discussed in the rejection, the court in *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), held that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". While Appellants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. In the present situation, Appellants have provided only a disclosure of a wish to obtain homologues, mutant, allelic, and splice variants of SEQ ID NO: 7212. The specification does not disclose any specific mutant, allelic, or splice variants or homologues of SEQ ID NO: 7212. Further, the functional activity of such variants is not disclosed. Accordingly, the specification has not disclosed a representative number of nucleic acid molecules within the claimed genus.

Appellants assert that they have disclosed the common structural features of the claimed nucleic acids, i.e., SEQ ID NO: 7212. However, the claims are not limited to nucleic acids which share this common structural feature. Rather, the claims encompass nucleic acids having 90-99.9% identity with SEQ ID NO: 7212. Thereby, the claimed genus of nucleic acids do not share the same common structural feature of containing the sequence of SEQ ID NO: 7212. Appellants have not disclosed what specific sequence information must be shared by the claimed genus of nucleic acid molecules in order to ascertain which nucleic acids share a common structural feature. The genus of molecules having 95-99.9% identity with SEQ ID NO: 7212 includes individual species of nucleic acids which may vary from SEQ ID NO: 7212 at any given nucleotide position within SEQ ID NO: 7212. When the individual species within the genus are compared to one another, together this genus comprises nucleic acids which vary at each and every nucleotide position within SEQ ID NO: 7212. Accordingly, the genus of nucleic acids are not considered to share a common structural feature – i.e., there is no specific structural property that is common to all members of the claimed genus if each of the individual nucleotides may be varied. Further, the claims do not recite a functional requirement for any of the claimed nucleic acids and thereby encompass nucleic acids having distinct functional properties.

At page 17, Appellants state that "closely related nucleic acid molecules falling within the scope of the invention are readily identifiable – they either contain the nucleic acid sequence of SEQ ID NO: 7212 or share a claimed identity with SEQ ID NO: 7212, or they do not. The fact that the nucleic acid molecules may comprise additional

sequences or variations is beside the point. Such modifications are readily envisioned by one of ordinary skill in the art and disclosed throughout the specification. Thus, contrary to the Examiner's analysis, claims 1, 8-12 are supported by an adequate written description." These arguments have been fully considered but are not found persuasive. It is noted that the criteria for meeting the Written Description requirement is not limited to providing a means for distinguishing between molecules which fall within the claimed genus and molecules which fall outside the claimed genus. Rather, the Written Description requirement is met by providing a showing that Appellants were, at the time the application was filed, in possession of the claimed invention. Providing a statement that the invention covers nucleic acid having 90-99.9% identity with SEQ ID NO: 7212 is not equivalent to disclosing specific nucleic acids which fall within the claimed genus of nucleic acids. The specification does not disclose a single molecule within the genus of nucleic acids having 90-99.9% identity with SEQ ID NO: 7212. The specification does not describe the location or identity of nucleotides which may be varied within SEQ ID NO: 7212, and does not describe the functional activity or other biological role associated with such variants. The specification also does not disclose any specific variants of SEQ ID NO: 7212 which have a functional activity or biological role distinct from that of SEQ ID NO: 7212. Modification of a nucleic acid sequence by 1 to 10% can significantly alter the functional activity of the nucleic acid and the protein encoded thereby. The genus of nucleic acids claimed is large and variable, and potentially includes nucleic acids encoding for proteins having diverse biological functions. The specification discloses only one member of this genus, i.e., SEQ ID NO:

7212. This is not sufficient to place one of skill in the art in possession of a representative number of molecules having the varied attributes and features of species within the claimed genus. Accordingly, it is maintained that the written description requirements have not been adequately met for the broadly claimed genus of homologues, splice, mutant and polymorphic variants of SEQ ID NO:7212.

Appellants further argue that Claims 1, 12 are separately patentable, however, each of these claims are drawn to sequences minimally comprising SEQ ID NO: 7212. As noted in the rejection above, the claims recite open transitional language ("having"; "comprising"), and therefore include, e.g., molecules that are 90-100% identical with SEQ ID NO: 7212 and which further include undefined flanking sequences. the claims recite open transitional language ("having"; "comprising"), and therefore include, e.g., molecules that are 90-100% identical with SEQ ID NO: 7212 and which further include undefined flanking sequences. For the above reasons, it is believed that the rejections should be sustained.

Conclusion

7. No claims allowable.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.

J. Goldberg

Jeanine Goldberg
Primary Examiner
February 6, 2007